REMARKS

The above amendments have been provided based on the format described at 1265 Off. Gaz. Pat. Office 87 (December 17, 2002) and as authorized by Deputy Commissioner for Patents, Stephen Kunin on January 31, 2003.

Claims 1-20 were pending. The Examiner withdrew 1-10 and 16-20 from consideration following a restriction requirement. Claims 11-15 were rejected in the previous Office action, and no claims were allowed. Claims 11, 12, and 15 are amended herein. New claims 21 and 22 have been added. Support for new claim 21 is found in the specification at page 46, lines 33-34 and page 48, lines 10-21. Support for new claim 22 is found in the specification at page 48, lines 28-30. It is believed that no new matter has been added. Please cancel claims 1-10 and 16-20 without prejudice. Claims 11-15 and 21-22 are currently pending.

Formal Matters

Applicants gratefully acknowledge the rejoining of Groups VI, VII, and VIII by the Examiner.

The Examiner alleges that the application filed under former 37 C.F.R. § 1.60 lacks the current status of the nonprovisional parent application 09/351,777. Applicants note that this paragraph was properly amended in the preliminary amendment submitted April 23, 2001 to reflect priority claims. Nonetheless, the first paragraph has been amended again herein to reflect the status of the application as a continuation of the parent application, Serial No. 09/351,777.

The Examiner objects to the specification referring to SEQ ID NOs:12-19 as Table 4 because they are not in tabular form and are duplicates of the sequence listing. The specification is amended herewith deleting Table 4.

The Examiner alleges claims 11 and 12 recite non-elected inventions. Claims 11 and 12 are amended herein to recite elected inventions.

In light of the above, Applicants respectfully submit that the objection to the specification has been overcome. Therefore, Applicants request the withdrawal of the objections.

Rejection Under 35 U.S.C. §§ 101 and 112

Claims 11-15 are rejected under 35 U.S.C. §§ 101 and 112 as allegedly lacking the support of either a specific and substantial asserted utility or a well established utility. According to the Examiner, the involvement of the RANKL receptors in cell proliferation or differentiation or involvement with any disease or disorder is conjectural. The Examiner asserts that in view of the absence of any information about the biological significance of RANKL or its receptor, the antibody binding compounds lack any specific diagnostic or therapeutic use. Applicants respectfully traverse this rejection for reasons discussed below.

The specification provides at least one specific, substantial, and credible utility based on the sequence homology to existing members of the TNF receptor family and the expression of RANKL in inflammatory responses. Applicants note that according to the Utility Examination Guidelines "[w]hen a ... [protein] is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein." 66 Fed. Reg. 1092, 1096 (2001). At page 30, lines 15-22, the specification discloses the homology between RANKL and the TNF receptor. The specification also discloses the expression of RANKL in inflammatory responses. Under the Utility Guidelines cited above, the known specific, substantial, and credible utility known for the TNF receptor family members, particularly for inflammatory and allergic responses and associated diseases, is sufficient to meet the standard set under 35 U.S.C. §§ 101 and 112.

Based on the disclosed homology to the TNF receptor family, Applicants have specifically asserted at least one specific, substantial and credible utility for RANKL sufficient to satisfy 35 U.S.C. §§ 101 and 112. For example, the Examiner's attention is directed to page 57, lines 8-25. The specification clearly states that antibodies to RANKL "should be useful in the treatment of conditions associated with abnormal physiology or development, including abnormal proliferation." See specification, page 57, lines 13-15. The specification then cites the

modulation of the development of lymphoid cells in particular" as one use for reagents that bind RANKL. See specification, page 57, lines 16-18 (emphasis added). The specification goes on to state that "[RANKL] plays a role in regulation or development of hematopoietic cells ... lymphoid cells, which affect immunological responses." *See* specification, page 57, lines 22-24. In view of the disclosure in the specification, RANKL's homology to known TNF receptor family members would lead the skilled artisan to expect RANKL to participate in immunological responses associated with abnormal proliferation of hematopoietic cells.

Furthermore, the specification discloses evidence of the utility of RANKL in inflammatory and allergic responses, *i.e.*, immunological responses associated with abnormal proliferation of hematopoietic cells. At page 30, line 32, the specification discloses that the expression of RANKL in the lungs of allergic guinea pigs is observed after a 3 day autoradiograph exposure. RANKL expression is not detected in the normal guinea pig lung after a 3 day autoradiograph exposure, but requires a 14 day exposure to detect RANKL expression. *See* specification at page 30, line 37. A similar pattern is observed in a monkey allergic lung model. The specification discloses the expression of RANKL is observed in a 3 day autoradiograph of allergic monkey lung, while a 14 day autoradiograph is required to detect RANKL expression in a normal monkey lung. *See* specification at page 31, lines 2-7. It is known to the skilled artisan that higher expression is detectable in shorter (*e.g.*, 3 day) autoradiograph exposures while low expression requires longer autoradiograph (*e.g.*, 14 day) exposures. Thus, in two different animal models for inflammation/allergy models, RANKL is highly expressed in allergic lung with little expression in normal lung.

The Declaration of Ms. Jeanine Mattson submitted herewith further demonstrates the expression of RANKL in inflammatory responses associated with abnormal proliferation of hematopoietic cells, *e.g.*, lymphocytes and macrophages in the lung. The data demonstrate the greatly increased expression of RANKL in human lung taken from patients with idiopathic pulmonary fibrosis. Proliferating lymphocytes and macrophages are recognized as the mediators of the lung pathology observed in this lung disease. *See* Exhibit A. Using real time PCR

analysis, Ms. Mattson shows that RANKL expression is greater than 20 fold higher in the lung from patients with idiopathic pulmonary fibrosis than that observed in lung from normal individuals. *See* Declaration of Jeanine Mattson, Table 1. Similarly, in an animal model for inflammatory responses, the data in Ms. Mattson's declaration further demonstrates the expression of RANKL in another system associated with abnormal proliferation of hematopoietic cells, *i.e.*, the lungs of *C. macaque* following *Ascaris* challenge. *Ascaris* is a parasitic nematode that elicits a granulomatous inflammation in the lung in infected individuals. *See* Exhibit B. The inflammation observed in the lungs following *Ascaris* challenge is associated with abnormally proliferating lymphocytes and macrophages. Using real time PCR analysis, Ms. Mattson shows that RANKL expression is greater than 9 fold higher in the lung from monkeys challenged with Ascaris relative to that observed in normal lung. *See* Declaration of Jeanine Mattson, Table 2. Thus, this data confirm the expression of RANKL in disease mediated by abnormally proliferating hematopoietic cells.

Taken together, the specification discloses that RANKL's homology to other members of the TNF receptor family and specifically asserts a specific utility in immunological responses associated with abnormal proliferation of hematopoietic cells. The data summarized above demonstrate the expression of RANKL in human disease and animal models of inflammation mediated by the abnormal proliferation of hematopoietic cells.

Finally, the utilities disclosed in the specification are credible to one of skill in the art. Textbooks relied upon by skilled artisans recite the abnormal proliferation of hematopoietic cells as a cause of the pathology observed in the human disease and the animal model where RANKL is expressed. *See* Exhibits A and B. Furthermore, RANKL is a member of the TNF receptor superfamily, a well-defined cytokine receptor family known to participate in the regulation of hemtapoietic cell proliferation and viability. Therefore, the skilled artisan would recognize and believe the utilities disclosed in the instant application and thus meet the utility requirement set forth under 35 U.S.C. §§ 101 and 112.

In light of the above remarks, Applicant respectfully submits that the rejection under 35 U.S.C. §§ 101 and 112 is overcome. Therefore, Applicants request the withdrawal of this rejection.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 11-15 are rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. According to the Examiner, it is not clear what "specifically" binds means in claim 11. The Examiner also asserts that the recitation of "selectively" immunoreactive is not clear in claim 12. The Examiner further states that claim 12 recites the binding compound is a polyclonal antiserum, and a polyclonal antiserum is not a compound but is composed of many compounds. The Examiner alleges that claim 15 is indefinite because it encompasses a detection kit comprising a binding compound and a compartment providing segregation of the binding compound, and it is not clear what it is being segregated from. Applicants respectfully traverse the rejections for the reasons discussed below.

The term "specifically" in claim 11 has its ordinary meaning in the art. "The specificity of an antibody determines its ability to distinguish the immunogen from other antigens." JANEWAY, ET AL., IMMUNOBIOLOGY 704 (5th ed. 2001). In other words, a specific antibody is one that binds an epitope in the immunogen used to elicit the antibody response. It is well known in the art that if epitopes of an immunogen are shared within other species, the antibody may also bind the same immunogen from another species. However, this does not alter the definition of "specificity" for an antibody in the least because the antibody remains specific for a single epitope. Applicants have not sought to give any new meaning to the word "specificity," thus the claim term is sufficiently definite given the accepted meaning for the term.

Likewise, the term "selectively immunoreactive" has its ordinary meaning in the art. The claimed binding compound binds the claimed polypeptide through interaction with its antigen binding site. Nonetheless, to expedite prosecution, Applicants have deleted "selectively" from claim 12.

Applicants respectfully submit that polyclonal antiserum of claim 12 is sufficiently definite to meet the standard set forth under 35 U.S.C. § 112, second paragraph. However, to expedite prosecution, the term "polyclonal antiserum" has been amended to indicate the binding compound is present in polyclonal antiserum.

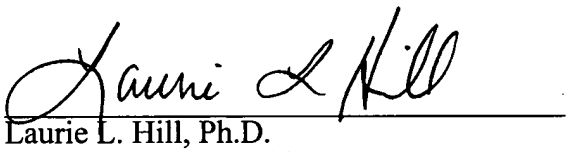
Claim 15 has been amended herein to clarify that the claimed compartment provides segregation of the claimed binding reagent from other kit reagents.

In light of the above remarks, Applicant respectfully submits that the rejection under 35 U.S.C. § 112, second paragraph is overcome. Therefore, Applicants request the withdrawal of this rejection.

CONCLUSION

Applicants submit that the objections and the rejections under 35 U.S.C. §§ 101 and 112 have been overcome by the above amendments and remarks. Early allowance of pending claims 11-15 and 21-22 is respectfully requested. In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 140942000401.

Respectfully submitted,

Dated: April 28, 2003 By: 

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